To: Providers of Women's Health Care
From: Office of the Special Assistant for Women's Health, BUMED

Re: Information about Bone Loss with the Use of Depo-Provera

In NOV04, the FDA and Pfizer announced warnings to healthcare providers about the loss of bone mineral density (BMD) with the use of depo-medroxyprogesterone acetate (DPMA or Depo-Provera). The "black box warning" for Depo-Provera highlights that prolonged use of the drug may result in significant loss of bone density and that the loss is greater the longer the drug is administered. This bone density loss may not be completely reversible after discontinuation of the drug. Thus the warning states that a woman should only use Depo-Provera Contraceptive Injection as a long-term birth control method (for example, longer than two years) if other birth control methods are inadequate.

The following is the link for more information about the FDA and Pfizer warnings: http://www.fda.gov/medwatch/SAFETY/2004/safety04.htm#Depo.

The pertinent clinical research articles on this topic are available on the Women's Health webpage on NMO (http://navymedicine.med.navy.mil/).

A prospective longitudinal study done by Clark et al. at the University of Iowa released in Fertility and Sterility in DEC04 confirms substantial loss of bone with the contraceptive DPMA use. The study involved 178 first-time users of Depo-Provera and 145 women not using hormonal contraception between the ages of 18-35. The group of women taking Depo-Provera experienced a mean bone mineral density (BMD) loss at the hip of nearly 2.8%, just one year after starting the DMPA injections. This number increased to 5.8% mean BMD loss after two years of injections. The loss of bone density in the spinal region showed similar results. On the other hand, the women who didn't take hormonal contraception (control group) exhibited 0.9% bone loss at the hip and spine, which is a significantly lower drop in the mean BMD. The BMD loss in the spine decelerated somewhat after 18 months of DMPA use while the BMD loss was linear for the hip. Other studies of long-term users of DMPA suggest that BMD loss may attenuate after 2 years. Physical activity and calcium intake did not offer protection in the study. Only increased body mass index (BMI) seemed to be somewhat protective of the spine. The results of another study by Scholes et al. that followed women after DMPA discontinuation suggests that BMD may return to normal about 30 months following discontinuation. The average BMD loss observed in the University of Iowa study is such that, if not recovered, would lead to an increased risk for osteoporosis and fracture following menopause. In postmenopausal women, BMD decreases of 5% have increased the fracture risk by 50%. In summary, women using DMPA began losing BMD after the first injection and continued losing BMD for up to 2 years of use in this study.

Currently, the **DoD formulary will not be affected** by this "black box warning" and Depo-Provera will be available for providers to prescribe for women, if clinically indicated.